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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/591,561	06/13/2000	Martin B. Wax	P-3023-US1	7525

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Mark S Cohen
Eitan Pearl Latzer & Cohen-Zadek
One Crystal Park Ste 210
2011 Crystal Drive
Arlington, VA 22202-3709

EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/591,561	WAX ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *3-10 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,11-14,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-17* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-17 are pending in the instant application.

Claims 1, 2, 11-14, 16 and 17 are under examination.

Claims 3-10 and 15 are withdrawn as directed to a non-elected invention.

Oath/Declaration

2. The oath or declaration is defective for reasons of record in the previous Office Action, Paper No. 8, page 3. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. On page 2 of the amendment filed June 17, 2002, Applicants stated that they would provide an Oath and Declaration claiming benefit under 35 USC 120 to Application U.S. Serial No. 09/500,023, but until such Oath and Declaration is provided the objection is maintained.

Priority

3. Applicants' amendment to the specification to recite the priority claimed in the declaration is acknowledged.

Specification

4. The objection to the disclosure is maintained because of the following informalities: in the legend to Figure 13 on page 9, on the third line is written "TNF-□", which should be changed to "TNF- α".

Appropriate correction is required.

Withdrawn Rejections

5. The rejection of claims under 112 § 2 is withdrawn in view of Applicants' amendment.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 11, 16 and 17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 16 and 17 of copending allowed Application No. 09/500,023. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of both applications are drawn to a method for treating a subject with glaucoma comprising the steps of administrating a compound or composition containing an agent or molecule which antagonizes, inhibits, inactivates, reduces, suppresses, and/or limits the release, synthesis, or production of TNF-α from cells.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. The rejection of claims 1, 2, 11, 12, 13, 16 and 17 are maintained under 35 U.S.C. 102(e) as being anticipated by Ron et al., PN 6,204,270, for reasons of record in the previous Office Action, Paper No. 8, at pages 4-5.

Applicants traverse the rejection and assert that Ron et al. does not disclose Applicants' invention, and that claim 1 is directed to a method for treating a subject with glaucoma by administering to the subject an amount of a compound or molecule which antagonizes, inhibits, inactivates, reduces suppresses and/or limits the release, synthesis or production of TNF-α. Applicants assert that Ron et al. does not teach a method of treating a subject with glaucoma by using a compound or molecule which antagonizes, inhibits, inactivates, reduces, suppresses and/or limits the release, synthesis or production of TNF-α, and that Ron et al. does not raise to the level of an anticipatory reference since Ron does not provide any, much less credible scientific data and/or experiments directed to the use of anti-TNF-α for treatment of a subject having glaucoma. Applicants point out that Ron specifically discusses anti-TNF-α treatment for mucosal inflammatory disease, but that glaucoma is not a mucosal disease nor an inflammatory disease. Applicants also assert that there has never been any evidence of immune complex deposition, retinal exudates, compliment proteins of T cell deposits in the retinas of any

glaucoma specimen as demonstrated by histopathology which are the hallmarks of inflammation but not present in glaucoma, and that Ron provides no experimental data and/or evidence to support or suggest any credible basis for such a disclosure. Applicants point out that prior to Applicants' invention there was no understanding or appreciation of the role of TNF in regard to glaucoma, and one skilled in the art would not have known that the TNF inhibitory compounds may be used to treat a subject with glaucoma. Applicants assert that they first showed the involvement of TNF-alpha mediated cell death in glaucoma, and the neuroprotective effect of anti-TNF-alpha treatment on the retinal ganglion cell survival, and by immunohistochemistry that the optic nerve head region through which the retinal ganglion cell axons pass as they exit the eye is accompanied by increased matrix metalloproteinase activity and increased TNF-alpha expression in glaucoma eyes, which discovery allowed Applicants to perform unique *in vitro* studies in which they provided evidence that it is the non-neuronal glial cells in the retina that directly cause the death of neuronal ganglion cells in response to stressors identified in glaucomatous eyes such as elevated pressure and ischemia.

Applicants' arguments have been considered but are not persuasive. Though Applicants have demonstrated underlying molecular events involved in glaucoma, the invention as broadly claimed reads on the prior art. Ron et al teaches that TNF-α may mediate various ocular disorders including glaucoma, and teach methods of treatment and compositions comprising anti-TNF-α antibodies. Since Ron et al. teaches that glaucoma can be treated by compounds that inhibit TNF-alpha, there was an understanding of the role of TNF in regard to glaucoma. For a reference to be anticipatory, it need only teach what is being claimed. In this case, Ron et al.

teaches that glaucoma can be treated with inhibitors of TNF-alpha activity. Therefore, Ron et al. anticipates the claims, and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 14 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Ron et al., PN 6,204,270, and further in view of Tobinick, PN 6,177,077, for reasons of record in the previous Office Action, Paper No. 8, at pages 5-6.

Applicants traverse the rejection and assert that it would not have been obvious to obtain Applicants' invention based on the disclosure alone or in combination of Ron et al and further in view of Tobinick. Applicants' further assert that the Examiner has not raised a *prima facie* case of obviousness, and since Ron et al. is not an anticipatory reference, Tobinick alone does not render obvious Applicants' claimed invention. Applicants' assert that it would not have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, to use infliximab or any other compound or molecule which antagonizes, inhibits, inactivates, reduces or suppresses and/or limits the release, synthesis or production of TNF-α in the method of treating glaucoma.

Applicants' arguments have been considered but are not persuasive. Since Ron et al. teaches that TNF-α may mediate various ocular disorders including glaucoma, and teach methods of treatment and compositions comprising anti- TNF-α antibodies, and Tobinick teaches that the commercially available chimeric anti-TNF monoclonal antibody infliximab is a specific inhibitor of TNF, and may provide the possibility of therapeutic intervention in TNF mediated diseases, it would have been *prima facie* obvious to a person of ordinary skill in the art of cytokines and their receptors at the time the invention was made, to use infliximab to treat glaucoma. One of skill would be motivated to do so, because infliximab is a readily available commercial pharmaceutical that has been demonstrated to be effective in inhibiting the effects of TNF-alpha, and the skilled artisan would have a reasonable expectation of success because of the effectiveness of the compound in treating other TNF-alpha related diseases or disorders. Therefore, the rejection under 35 USC 103 is maintained.

Advisory Information

If Applicants could supply evidence in the form of a declaration or articles, and directly addressing why the Ron et al. and Tobinick patents are not enabled for methods of treating glaucoma with antibodies that inhibit Tumor Necrosis Factor alpha, such declaration or showing could possibly overcome the prior art rejections, as was done for parent application 09/500,023.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

Yvonne Eyler

YVONNE EYLER, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600